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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,045	07/12/2001	John W. Butcher	20709	1941
210	7590	04/02/2004	EXAMINER	
MERCK AND CO INC P O BOX 2000 RAHWAY, NJ 070650907			CEPERLEY, MARY	
		ART UNIT	PAPER NUMBER	
		1641		

DATE MAILED: 04/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/904,045	BUTCHER ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Mary (Molly) E. Ceperley	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM  
 THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) Responsive to communication(s) filed on 23 January 2004.  
 2a) This action is FINAL.                  2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) Claim(s) 5-27 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 5-27 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____ .  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ .   | 6) <input type="checkbox"/> Other: _____ .                                  |

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**1)** A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

**2)** The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

**3)** Claims 5-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over **a)** Baldwin et al (U.S. Patent No. 5,633,247) taken in combination with each of **b)** Chadwick et al (Circulation Research, Vol. 72, No. 3, page 707 (1993)), Fiset et al (J. Mol. Cell Cardiol., Vol. 28, page 1085 (1996)), Geonzon et al (J. Mol. Cell Cardiol., Vol. 30, page 1691 (1998), or Duff et al (Circulation Research, Vol. 77, page 718 (1995) and with **c)** Dean et al (Synthesis and Applications of Isotopically Labelled Compounds, Paper 140 (1994)). This rejection is made for the reasons set forth in the first Office action (see below) and as further amplified in the final rejection and advisory action.

Baldwin et al describe the non-radiolabeled, sulfonamide compound of formula I of instant claim 1 as being a known Class III, K<sup>+</sup> channel blocking antiarrhythmia agent. See TABLE LVIII, Example 447 of col. 208; col. 2, lines 51-54; col. 19, lines 14-40 and 1-6.

Another Class III, K<sup>+</sup> channel blocking antiarrhythmia agent is the sulfonamide-containing drug Dofetilide (for the structure of Dofetilide, see fig. 3 of Vandenberg et al, cited by applicants on form PTO-1449). Each of references **b)** describes an assay which assesses the membrane K<sup>+</sup> channel blocking activity of radiolabeled [<sup>3</sup>H] Dofetilide. See Chadwick et al: abstract, guinea pig cardiac myocytes; page 708, [<sup>3</sup>H] Dofetilide Binding, Fiset et al: page 1086, "[<sup>3</sup>H]dofetilide equilibrium binding assay" using

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myocytes, membrane homogenates, or CHO cells; Geonzon et al: Figure 1; Duff et al: page 719 "Kinetic Binding Assays". Duff et al, in the table of page 719, define  $I_{KR}$  consistent with the usage of this term in the instant specification.

Dean et al describe the use of a  $^{35}S$ -containing sulfonamide group as being an improvement over  $^{125}I$  and tritium labels for sulfonamide-containing ligands used in receptor binding radioassays. See the Summary, Introduction, and the last paragraph of page 800.

Given the fact that conventional radioassays which utilize the  $I_{Kr}$  channel blocking activity of Class III antiarrhythmia agents are well known (references **b**), it would be obvious to substitute another well known Class III antiarrhythmia agent, namely the sulfonamide compound of Baldwin et al, in the methods of references **b**, as claimed, with the expectation of obtaining an equivalently useful assay method. The substitution of a  $^{35}S$  label for a  $^3H$  label in the Baldwin et al compound would be an obvious improvement given the teachings of Dean et al that a  $^{35}S$  label is preferred over a  $^3H$  label in radioassays involving sulfonamide derivatives.

The additional limitations/features of the claims are either specifically described by the references (e.g. for the use of the CHO cells of claim 7, see Fiset et al; for the specific activity of claim 9, see Dean et al; for competitive binding of test compounds in a radioassay, see Fiset et al, page 1089, "Class III antiarrhythmic drugs binding to [ $^3H$ ]dofetilide binding site") or constitute obvious variations in parameters which are routinely modified in the art (e.g. standard assay protocol of claim 10 using controls and test solutions of varying concentrations) and which have not been described as critical to the practice of the invention.

**4)** To advance prosecution, applicants should address the remarks made by the examiner in paragraph **1)** of the advisory action.

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**5)** An inquiry of a general nature which is **not related to the prosecution on the merits** should be directed to Technology Center 1600 telephone number (571) 272-1600. The general fax number for the USPTO is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary (Molly) E. Ceperley whose telephone number is (571) 272-0813. The examiner can normally be reached from 8 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le, can be reached on (571) 272-0823.

April 01, 2004

*Mary E. Ceperley*  
Mary (Molly) E. Ceperley  
Primary Examiner  
Art Unit 1641